

REMARKS

Claims 68-76 were added in the previous Amendment. In the Examiner's view these claims are drawn to a invention that is independent or distinct from the invention of previously pending claims 51-60. Accordingly, the Examiner has issued a restriction of the claims to two groups:

Group I: Claims 51-60, drawn to a device in which the labeled reagents do not bond to the analyte; and

Group II: Claims 68-76, drawn to a device in which the labeled reagent binds to the analyte.

The Examiner has asserted that the claims of Group I have been constructively elected by their original presentation and receipt of an action on the merits. (Paper No. 20090201 at 2.)

Accordingly, claims 51-60 are currently under examination.

35 U.S.C. § 103

Claims 51-60 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Fitzpatrick *et al.*, U.S. Patent 5,451,504 ("*Fitzpatrick*") in view of Guirguis U.S. Patent Application Publication 2002/0160538 ("*Guirguis*"). (Paper No. 20080201 at 3.) In making the rejection, the Examiner has equated *Fitzpatrick's* mobilization zone with the sample application zone of the invention, *Fitzpatrick's* trap zone with the test zone of the invention, and *Fitzpatrick's* detection zone with the reference zone of the invention. (See *Id.*) The Examiner has characterized the trap zone of *Fitzpatrick* as having "an immobilized ligand (that binds to the labeled reagent when analyte is not present producing a signal that is inversely proportional to the concentration of analyte)" and that the detection zone "provides for detection of a receptor-analyte complex which positively correlates with the presence of analyte in the sample." (*Id.*)

The Examiner has acknowledged that *Fitzpatrick* differs from the claimed invention in that it is "silent as to the detection of analyte concentration and . . . does not specifically teach that the different zones of the test strip contains a pre-determined amount of reagents which is based upon the pre-determined range of analyte concentration." (*Id.* at 4.)

To close this gap, the Examiner has relied on *Guirguis* as teaching "a test strip where one or more reagents are immobilized in a corresponding number of reaction zones [and] . . . that a desired amount of capture reagent can be immobilized in the reaction zone, and that a threshold concentration of bound reagent may be used to detect a predetermined amount of analyte." (*Id.* at 4.) The Examiner has further alleged that:

Guirguis teaches that threshold concentration includes the lower limit of a concentration for an analyte. Guirguis also teaches a device including several reaction zones, each reaction zone including a different threshold concentration for the same analyte. In this embodiment, the threshold concentration provides a reference point for determining the upper limit of an analyte concentration range.

(*Id.* at 5.) The Examiner has concluded that "it would have been obvious . . . to immobilize a predetermined amount of capture reagents in the different zones of the device of *Fitzpatrick* as taught by *Guirguis* because the process for using predetermined amount of assay reagents based upon a predetermined range of analyte is well known in the art as clearly taught by *Guirguis*." (*Id.*) Applicants respectfully traverse the rejection.

The instant claims recite "pre-determined amount[s of the first and second reagents] . . . based on the pre-determined range of analyte concentration" and that "the pre-determined amount of the . . . reagent such that the detectable response is" inversely or directly proportional to the analyte concentration, respectively. The rejection is deficient for at

least three reasons: 1) even in combination, *Fitzpatrick* and *Guirguis* do not disclose any detectable response that is inversely or directly proportional the analyte concentration; 2) *Guirguis* explicitly teaches away from the claimed flow through devices; and 3) the proposed combination would render the devices inoperable purposes taught in *Fitzpatrick*. Accordingly, the rejection provides no rationale for one of skill in the art to modify the prior art in the manner required to arrive at the claimed invention. Thus, the rejection does not present a *prima facie* case for the obviousness of the presently claimed assay devices.

Fitzpatrick discloses a membrane strip with three general zones: a mobilization zone, a trap zone, and a detection zone. (See Abstract; col. 1, lines 46-69; col. 2, lines 15-16; and col. 4, line 50 - col. 9, line 15.) *Fitzpatrick* is silent as to any detectable response in its trap zone. This trap zone "comprises immobilized ligand that will bind, i.e., trap, free receptor moving through the trap zone, but will not bind receptor bound in a receptor-analyte complex." (col. 6, lines 39-41.) In nearly two full columns of text devoted exclusively to the trap zone, *Fitzpatrick* says absolutely nothing about any detectable response, much less any inversely proportional response.

Moreover, *Fitzpatrick* discloses only that the response in the detection zone has a positive correlation to the presence of the analyte. *Fitzpatrick* actually emphasizes the desirability of a simple signal that only reflects a positive result.

Positive detection means that signal positively correlates with the presence of analyte in a sample. **A positive correlation is advantageous because it is psychologically satisfying that the presence of signal or increase in signal intensity indicates presence of analyte in a sample.** Both sophisticated diagnostic laboratories and non-technical personnel **benefit from**

the use of an assay in which a signal means only a positive result because such results are not susceptible to misinterpretation, as may occur when the absence of signal indicates presence of analyte.

(Col. 8, lines 19-29 (emphasis added).)

In sum, *Fitzpatrick* is concerned only with the detection of "the presence [or absence] of an analyte in a sample" (Abstract) by use of a positively correlated response and nothing more. *Fitzpatrick* is completely silent as to any proportional response in the trap or detection zones, as is required in the claimed reference zone. In the sole example in *Fitzpatrick*, the results are reported only as negative or positive for the detection of the analyte. (See Table 1 and col. 13, lines 21-48.) Thus, *Fitzpatrick* does not teach any proportional response in its detection zone or any inversely proportional response in its trap zone, as claimed.

Guirguis is devoid of any teaching that closes this gap in *Fitzpatrick*. *Guirguis* teaches an "assay device and method, . . . which allow the determination of the presence or absence of at least one analyte in a test sample, while providing specific identification of the test subject. The assay device includes a reaction medium having at least one reaction zone and at least one control zone, which is capable of providing a pattern suitable for identifying the test subject." (Abstract.) *Guirguis* explicitly teaches away from the "flow through" devices (e.g., the test strips) of *Fitzpatrick*:

The methods and devices according to the invention are particularly beneficial in that ***only a small amount of signal-producing agent is required, in contrast to the conventional flow through cassettes or devices;*** applying pressure while maintaining direct contact on the surface of the test device maintains a localized concentration of reagents, particularly the signal-producing agent, which ***appears to increase the speed and sensitivity of the reaction, e.g., test results are obtained in a matter of seconds versus a matter of minutes or longer;*** and, in some embodiments, labeling a secondary antibody (as opposed to

labeling the primary antibody or the antigen) decreases the reaction time of the assay because the antigen's shape is not altered by being bonded to a label.

(¶ 0021 (emphasis added).)

Guirguis also teaches "devices for rapidly determining the quantitative amount of an analyte in a sample" (¶ 0013.) To achieve this goal, *Guirguis* teaches that:

One skilled in the art will recognize that a desired amount of antigen can be immobilized in the reaction zone, and that a threshold concentration of bound [immunological pair ("MIP")] may be used to detect a predetermined amount of analyte. . . . As used herein, threshold amount or concentration refers to the lower limit of a concentration range for an analyte. In another embodiment of the invention the detection device includes several reaction zones, each reaction zone including a different threshold concentration for the same analyte. ***In this embodiment, the threshold concentration provides a reference point for determining the upper limit of an analyte concentration range.***

(¶ 0109 (emphasis added).)

Thus, *Guirguis* teaches only devices providing one or more discrete results. For example, in the case of those devices with "a threshold concentration of bound MIP," the analyte is reported as present or not present in the minimum amount. Even in a device including "several reaction zones, each reaction zone including a different threshold concentration for the same analyte" only "the upper limit of an analyte concentration range" may be determined. For example, if the concentration thresholds are set at 1, 2, and 3 mg/ml, the device can only reveal whether the concentration of the analyte is less than or more than each threshold. In sum, *Guirguis* does not teach a proportional response, *i.e.*, as the concentration of analyte rises the signal increases (or decreases) proportionally, much less both directly and inversely proportional responses, as recited by the instant claims.

The routineer in the art is an objective legal construct, who is presumed to think along conventional lines, without undertaking to innovate, whether by systematic research or by extraordinary insights. See *Life Technologies Inc. v. Clontech Lab, Inc.*, 224 F.3d 1320, 1325, 56 U.S.P.Q.2d 1186, 1190 (Fed. Cir. 2000) (quoting *Standard Oil Co. v. American Cyanamid Co.*, 774 F.2d 448, 454, 227 U.S.P.Q. 293, 297 (Fed. Cir. 1985)). Even in combination, *Fitzpatrick* and *Guirguis* fall short of teaching the claimed invention and the rejection provides nothing to close this gap. And, one of skill in the art would have had no rationale to modify the apparatuses of *Fitzpatrick* and *Guirguis* (which have produce only discrete responses) to arrive at the claimed device with (directly and inversely) proportional responses.

Notwithstanding the fact that the cited prior art falls short of teaching the claimed invention, to arrive at the claimed invention, would also have required one of skill in the art to ignore the teachings of *Guirguis* that flow through devices are too slow and cumbersome for its intended uses and require far more signal-producing agent. Thus, contrary to the Examiner's assertion, *Guirguis* teaches away from a "test strip," as claimed.

Prior art publications must be evaluated in their entirety. It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art. See, *In re Mercer* 515, F.2d 1161, 1165-66, 185 U.S.P.Q. 774, 778 (C.C.P.A. 1975). This is particularly true when a reference teaches away from the claimed invention, as *Guirguis* does. *In re ICON Health and Fitness, Inc.*, 496 F.3d 1374, 1381, 83 U.S.P.Q.2d 1746, 1751 (Fed. Cir. 2007) (a "reference may be said to teach away when a person of

ordinary skill, upon reading the reference, . . . would be led in a direction divergent from the path that was taken by the applicant.").

In essence, to arrive at the claimed invention, one of ordinary skill in the art would have had to dismantle *Guirguis*' invention and import only its "threshold concentrations," while ignoring the explicit teaching that *Guirguis*' devices are superior to and cannot be the flow through devices claimed by the Applicants and taught by *Fitzpatrick*. One of skill in the art would have had no rationale to do so.

In addition, *Guirguis* teaches that its "methods and devices . . . are particularly beneficial in that only a small amount of signal-producing agent is required, in contrast to the conventional flow through cassettes or devices" (§ 0021.) "In many of these [prior art] devices, due at least in part to the limited sensitivity of the devices, relatively large amounts of oftentimes expensive reagents or of test sample are required to give accurate results." (§ 0007.)

Thus, even if the threshold concentrations of *Guirguis* were imported, one of skill in the art would have expected these threshold concentrations to be far lower than the concentrations required to be useful in producing results for the "relatively large amounts of test sample" used in the flow through devices of *Fitzpatrick* (and the claimed invention). Thus, the proposed modification of *Fitzpatrick* with *Guirguis* would render *Fitzpatrick's* devices inoperable for their intended purpose.

Such a modification is not obvious. See, *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984) (reversing the decision of obviousness on the ground that the proposed modification of the prior art would have rendered the claimed invention inoperable for its intended purpose). Accordingly, one of skill in the art would have had no rationale to make such a modification.

For the foregoing reasons, the rejection fails to present a *prima facie* case for the obviousness of the claimed assay devices. Withdrawal of the rejection is respectfully requested.

As it is believed that the rejection set forth in the Official Action has been fully met, favorable reconsideration and allowance are earnestly solicited. If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that she telephone Applicants' attorney at (908) 654-5000 in order to overcome any additional objections.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

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